

REMARKS

Further examination of claims 1-5, 7-10, 13-22, and 24-27 is reported in the present, final Office Action. Claims 1-3, 7-10, 13, 19, and 20-22 were rejected under 35 U.S.C. § 102(b), and claims 1-5, 7-10, and 13-27 were rejected under 35 U.S.C. § 103(a). Each of the rejections is addressed below.

First, applicants note that claim 1 has now been amended to specify that the compound used to facilitate uptake of the virus by the cell in the method of this claim is a charged compound selected from a polysaccharide, polylysine, acyclodextrin, diethylaminoethane, and polyethylene glycol. Support for this amendment can be found, for example, in original claim 14.

Rejection under 35 U.S.C. § 102(b)

Claims 1-3, 7-10, 13, 19, and 20-22 were rejected under § 102(b) as being anticipated by Hodgson et al. (Nature Biotechnology 14:339-342, 1996). As is noted above, claim 1, from which the other rejected claims depend, has now been amended to recite a method for introducing a virus into a cell *in vivo*, involving the use of a charged compound selected from the group consisting of a polysaccharide, polylysine, acyclodextrin, diethylaminoethane, and polyethylene glycol. Hodgson, which describes cell culture studies characterizing the effects of cationic lipids on the efficiency of retroviral transduction, does not even mention the use of such charged compounds for this purpose. Applicants thus respectfully request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-5, 7-10, and 13-27 were rejected under § 103(a) for obviousness over Hodgson et al. (Nature Biotechnology 14:339-342, 1996), in view of Dyer (J. Virol. 71:191-198, 1997), Marasco (U.S. Patent No. 6,143,520), and Mislick (U.S. Patent No. 5,783,566). This rejection is respectfully traversed.

The Office Action states that it would have been obvious to use HSV or HIV vectors in the methods of Hodgson, because Dyer and Marasco teach that these vectors are capable of transfecting a variety of tissues. In addition, the Office Action states there would have been a reasonable expectation of success in using dermatan sulfate or dextran sulfate in these methods, because Mislick teaches that glycosaminoglycans are abundant on the cell surface, and Dyer teaches that virions gain entry into cells by recognizing various receptors on the cell surface. Applicants respectfully disagree.

Hodgson, as is noted above, describes characterization of the effects of cationic lipids on retroviral transduction of cultured cells, and does not even mention use of the types of charged compounds required by the present claims for enhancing viral uptake by cells *in vivo*. Dyer, was discussed in applicants' last reply, does not describe *in vivo* methods, and in fact teaches away from such methods. In particular, the focus of Dyer is characterization of the contribution of cell surface components to the herpes simplex virus (HSV) infection pathway. Central to Dyer's study is the use of a mutant cell line, sog9, which does not produce glycosaminoglycans (GAGs), the natural cell surface receptors for HSV. Dyer found that exogenously added dextran sulfate enhanced infection of sog9 cells by HSV-1, but not HSV-2, leading to the conclusion that it was the absence of endogenous GAGs in these cells that enabled the identification of this difference between HSV-1 and HSV-2 (page 197, lines 28-29). Dyer did not suggest the use of dextran

sulfate to enhance infectivity *in vivo*, which is not surprising, given that Dyer's results were obtained using mutant cells that do not occur *in vivo*, and that it was only because of the fact that such mutant cells were used that Dyer was able to detect enhanced infectivity. Moreover, regarding the use of dextran sulfate to enhance infection of non-mutant cells, Dyer stated that it was well established that dextran sulfate normally inhibits infection of such cells by enveloped viruses (page 197, lines 1-6). Dyer thus teaches away from the presently claimed invention.

Mislick does not make up for the deficiencies of Hodgson or Dyer in supporting this rejection. Rather, Mislick further teaches away from the use of exogenous glycosaminoglycans to enhance viral infectivity *in vivo*. On this point, Mislick states:

When transfection is performed *in vivo*, glycosaminoglycans and other polyanionic species in the plasma can adversely affect the transfection efficiency. Transfection efficiency can be increased by lowering the plasma concentration of glycosaminoglycans... (column 6, lines 5-9; emphasis added).

Thus, based on the teachings of Mislick, those of skill in this art would seek to decrease, rather than supplement, exogenous glycosaminoglycan concentration if desiring to introduce viruses into cells *in vivo*.

Marasco also does not provide support for this rejection. This reference, which describes the use of lentivirus vectors, such as HIV vectors, for use in gene expression studies, nowhere suggests or provides motivation to enhance viral infectivity *in vivo* by use of a charged polysaccharide, polylysine, acyclodextrin, diethylaminoethane, or polyethylene glycol.

Thus, because none of the cited references, alone or in combination, suggests or provides motivation to carry out the claimed methods, applicants respectfully request that the rejection under § 103(a) be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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PATENT TRADEMARK OFFICE

Version of Claims with Markings to Show Changes Made

1. (Twice Amended) A method for introducing a virus into a cell *in vivo*, said method comprising contacting said cell with said virus and a charged compound that facilitates uptake of the virus by the cell, wherein said compound is selected from the group consisting of a charged polysaccharide, polylysine, acyclodextrin, diethylaminoethane, and polyethylene glycol.

15. (Amended) The method of claim 1 [14], wherein said charged polysaccharide is a glycosaminoglycan.

16. (Amended) The method of claim 1 [14], wherein said charged polysaccharide is a glycosaminoglycan analog.